Overdiagnosis and -treatment in Mammo Screening Programmes

By Roland Holland MD, PhD

Nowadays a heated debate is going on in the scientific literature and lay press on the possible overdiagnosis and consequently, overtreatment of screen-detected breast cancers.

„However, I oppose Zahl's theory of "spontaneous regression" of breast cancers."

Roland Holland MD, PhD
National Expert and Training Centre for Breast Cancer Screening, Radboud University Medical Center Nijmegen, Netherlands

This debate was launched recently by the paper of Per-Henrik Zahl stating that many of the cancers detected on screening mammography are harmless and will not progress to a life threatening disease. On the contrary they may spontaneously regress. As a consequence these cancers will be unnecessarily treated with all the detrimental effects for the patient. In other words, mammography screening detects a lot of subclinical cancers that will never become clinical. This type of overdiagnosis and overtreatment in the study of Dr. Zahl is estimated to be as much as 50%.

Another recent study of Karsten Jorgensen and Peter Gotzsche addressed the same issue. They claim that harmless invasive cancer is common and when detected in mammography screening programmes, it is unnecessarily treated. Based on a literature review they found that in population based mammographic screening programmes about one-third of the women were overdiagnosed, that is, their cancers would not have been causing symptoms and death. In a recent editorial in JAMA Laura Esserman et al. address the issue of overdiagnosis for both screening for breast cancer and prostate cancer. "The increase of early cancers detected in screening is not necessarily beneficial" the paper states. They conclude that the incidence of breast and prostate cancers has increased after the start of the screening programmes and has never returned to pre-screening levels, indicating that many of these screen-detected cancers are early stage and may be harmless.

On the other hand, mammography advocates are strongly criticizing the above studies, stating that despite of a low rate of possible overdiagnosis, results of population based mammography screening projects undoubtedly showed a significant decrease of breast cancer mortality during the past 15 to 20 years. However, in fact, none of the above studies opposing these results. They only draw the attention to the fact that a number of screen detected cancers are most likely biologically non-aggressive and will not lead to deaths if untreated.

When reading those studies one could ask, what is actually new in their results? Not much really. The Netherlands and Sweden were the two pioneer countries introducing population based mammographic breast cancer screening in the late seventies. The adverse effect by detecting biologically unimportant "harmless" cancers by mammography was that time already well known and expected. Pathologists were aware that about 30% of screen-detected DCIS are low-grade with a limited potential to progress to an invasive cancer and if they do the invasive tumour will be most likely also low grade with limited potential for progression.

Studies show that such a process may take 10 to 15 years. A woman above 60 years of age will unlikely to die from this disease. Also many of the grade I and some of the grade II invasive cancers are indolent growing tumours with low metastatic potential. Most of these so called dormant tumors are harboured within the group of small screen-detected cancers and constitute the excess incidence as a result of screening.

However, I oppose Zahl's theory of "spontaneous regression" of breast cancers. There is no scientific evidence for this assumption. During my more than 40 years praxis I saw not a single case of invasive cancer, neither DCIS with signs of full regression. Many of invasive or DCIS cases show extensive necrosis or stromal fibrosis but viable cancer cells can be always traced in these processes by careful histopathological and immunohistological examinations.

The important contribution of the cited papers above, however, is the estimate of the proportion of overdiagnosis based on different analyses, being between 30 to 50% of screen detected cancers.

In an earlier study Paul van der Maas, that time chairman of the Dutch Evaluation Team for Breast Cancer Screening at the University of Rotterdam, calculated the expected rate of "overdiagnosis" in the Netherlands screening project. The study showed that in only 27% of screened women did early mammographic detection prevent death by breast cancer. For the other 73% of true positives early detection will not change the patient's survival. This group includes 53% of women surviving breast cancer regardless of the mode of tumor detection, that is, by mammography, or on the bases of clinical symptoms. Supposedly their tumors had no or low metastatic potential and were adequately treated. Another 13% will die despite the early detection of their highly aggressive cancer. Finally, about 7% would die from other causes and would have never known they had breast cancer if they were not screened. One may consider these 7% of cancers as the cases of true overdiagnosis of the screening programme.

Population based mammographic screening programmes show consistently a close to 30% significant mortality decrease for the age cohort 50 to 74 years. Overdiagnosis by mammographic screening is a prerequisite to achieve these results as long as we cannot differentiate between biologically less important, none progressive tumors and those with high metastatic potential based on the presently available conventional mammographic and histopathological tumor characteristics. Sub-molecular techniques unrevealing the biologic characteristics, the genetic profile of cancer will probably be able to make this distinction in the future. Untill such information is not available, "overdiagnosis" of screening programmes is unavoidable.

References

Per-Henrik Zahl et al. The Natural History of Invasive Breast Cancer Detected by Screening Mammography. *Arch Intern Med, 2008; 168*

Jorgensen KJ, Gotszche PC. Overdiagnosis in Publicly Organised Mammography Screening Programmes: A systematic Review of Incidence Trends. *BMJ 2009; 339*

Esserman L, et al. Rethinking Screening for Breast Cancer and Prostate Cancer. *JAMA 2009;302*

Van der Maas PJ. Breast Cancer Screening Programme in the Netherlands: An Interim Review. *Breast 2001; 10*

Tabar L, et al. Mammography Service Screening and Mortality in Breast Cancer Patients: 20-year Follow-up before and after Introduction of Screening. *Lancet 2003; 361*

Smith, RA. The Ongoing Evaluation of Breast Cancer Screening. *Cancer 2004; 100*